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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,190	09/24/2002	Steve Yeaman	YOU 2 0081	8208

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EXAMINER	
HANLEY, SUSAN MARIE	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,190	YEAMAN ET AL.	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/14/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: There is no step for converting the cells from the immortalized state to the non-immortalized state.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 9 is drawn to a cell line for "for subsequent use for studying Type-2-diabetes." It is unclear if, when or how the cell line will be used. It is suggested that the phrase be changed to "appropriate for studying Type-2-diabetes."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 10 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Serre et al. (1998).

Serre et al. disclose the effect of Extendin-(9-39) peptide on the secretion of insulin by beta-pancreatic cells (p. 4448, right col., last paragraph) that have been unconditionally immortalized. (This disclosure covers claim 2, wherein Extendin is considered to be the "factor" and the cells are unconditionally immortalized. Pancreatic cells are an insulin associated tissue, covers claim 3.) The cells are maintained in a growth-arrested state in the presence of tetracycline. The removal of tetracycline causes the cells to resume proliferation due to the regulated expression of the simian virus 40 (SV-40) T antigen by a tetracycline operator/tetracycline Transactivator system (p. 449, "Results" column, first paragraph). The effect of addition of Extendin on insulin secretion was examined in growth-arrested (tetracycline absent; this disclosure meets the limitation of claim 8) and proliferating (tetracycline present) cells (p. see figure 5, p. 4452). The disclosure meets the limitation of claim 1 because immortalized is interpreted to mean that the cells are proliferating continuously. This is the case when tetracycline is added to the disclosed pancreatic cell culture. Thus, the disclosure by Sere et al. meets the limitations of claims 1-3 and 10.

Claims 1, 3-7, 9, 12, 14, 15 and 17-19 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Davis et al. (US 6,291,172).

Davis et al. disclose an immortal "hybrid" cell for identifying therapeutic agents for Type-2 diabetes (abstract; col. 18, lines 41-67; covers claims 1 and 9). The cybrid cell is

a transformed cell (meets claims 6 and 17-19) wherein the mitochondria DNA of a person having Type-2 diabetes (NIDDM) is transferred to insulin secreting cells (pancreatic) or insulin-responsive cells derived from adipose, hepatic, muscle or neural tissue (covers claims 3-5, 7, 12, 14 and 15). Davis et al. disclose that any of the cell lines can be immortal (col. 8, lines 19-42; meets claim 1 limitation). Davis et al. teach that a cybrid cell can be contacted with a contacting a potential therapeutic agent for NIDDM with cybrid cells and measuring a phenotypic trait in the cybrid cell that is affected by the mitochondrial defect. Measurement of the phenotypic trait includes assays for mitochondrial complex V activity or assays for reactive oxygen species (col. 18, lines 41-67) . The effect of the potential therapeutic agent on the phenotypic trait expressed by the cybrid cell is indicative of insulin activity because mitochondrial response is an indicator of glucose transport into cells (col. 4, lines 60-65 through col. 5, lines 1-12). Hence, claims 1, 3-7, 9, 12, 14, 15 and 17-19 are clearly anticipated by the disclosure by Davis et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 8, 10, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al. (US 6,291,172) or Sabia et al. (1990) or Ullrich et al. (WO 95/23231) in view of Baetge et al. (US 6,358,739) and Pincon-Raymond et al. (1991).

The disclosure by Davis et al. regarding an immortal "hybrid" cell for identifying therapeutic agents for Type-2 diabetes is discussed *supra*.

Sabia et al. teach the effect of the glucose transport inhibitor, cytochalasin B, on primary cell cultures prepared from human muscle. The assay was accomplished by measuring the effect of the inhibitor on hexose uptake in the disclosed muscle cell lines. The effect on hexose transport is indicative of the effect of insulin on the target tissue since insulin directs hexose and glucose transport (p. 539, bottom third of right column).

Ullrich et al. disclose that baby hamster kidney (BHK) cells have been transformed to co-express the insulin receptor (IR) and the receptor protein tyrosine phosphatase (RPTP-alpha and RPTP-epsilon) which are under the control of the insulin signaling pathway. The intended use of the transformed cells is the identification of compounds that modulate insulin receptor-type tyrosine kinase mediated signal

transduction through cell-based assays. The phenotype of the cells, that is cell morphology and adhesion properties, can be used as an indicator of insulin mediated signal transduction. (p. 5, lines 32-35 through p. 6, lines 1-20).

Davis et al. do not teach the use of conditionally immortalized cells for identifying modulators of insulin response. Neither Sabia et al. not Ullrich et al. disclose the utilization of immortalized or conditionally immortalized cells for the same purpose.

Baetge et al. disclose that it is desirable to employ immortalized cells for treatment of medical disorders because they have unlimited replicative capacity and avoid cellular senescence. Primary cells have a limited capacity to proliferate. Thus, cellular immortality allows for increased cellular lifespan which is especially desirous for cells that are in short supply (col. 1, lines 17-45). However, immortalized cells have a drawback in that that are capable of developing tumors (col. 1, lines 45-50). This drawback can be overcome by making the cells conditionally immortal, wherein immortalization is terminated by the removal of an endogenously supplied compound (col. 2, lines 15-30). Baetge et al. disclose that human primary cells such as pancreatic, hepatic, muscle and fat cells can all be made conditionally immortal (col. 6, lines 5-20).

Pincon-Raymond et al. disclose that immortalized muscle cell lines are advantageous in that they can be grown indefinitely as a single cell type, while primary cultures are always a mixture of myogenic cells and fibroblasts. However, immortalized muscle cell lines have the problem that their differentiation properties are often far from those of the primary cells from which they have been transformed. To overcome these problems, Pincon-Raymond et al. disclose a conditionally immortalized normal and

dysgenic mouse muscle cells by the SV40 Large T antigen that is under the vimentin promotor control. These cells can be switched from immortal to non-immortal cells having the same properties as the primary cell from whence it originated. These cell lines can be applied to pharmacology, transplantation and cell biology studies (abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ immortalized or conditionally immortalized cells to identity the effect on modulators of insulin on cells affected by insulin. The ordinary artisan would have been motivated to employ immortalized cells to take advantage of the ability to maintain large numbers of homogenous cells that can be difficult to obtain. The ordinary artisan would have been further motivated to employ conditionally immortalized cells to overcome some of the problem associated with continuously growing cells, as pointed out by Pincon-Raymond et al. Additionally, Pincon-Raymond et al. suggest that such cells be used for pharmacology studies. The ordinary artisan would have had a reasonable expectation of success that immortalized or conditionally immortalized cells could be successfully employed to identify the effect on modulators of insulin on cells affected by insulin because they have been successfully cultivated and utilized for transplantation into humans.

The following references are made of record:

US 6,392,118 B1 Hammand et al. May 21, 2002

US 5,795,726 A Glucksman M. August 18, 1998

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).